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EXAMINER

SKOWRONEK, KARLHEINZ R

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1631

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/540,277	Applicant(s) HONG ET AL.	
	Examiner KARLHEINZ R. SKOWRONEK	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 1-26 and 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 June 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/21/05; 4/12/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group IV (claims 27-30) in the reply filed on 13 May 2008 is acknowledged.

Claims 1-26 and 31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 13 May 2008.

Claim Status

Claims 1-31 are pending.

Claims 1-26 and 31 are withdrawn as being directed to a non-elected invention.

Claims 27-30 have been examined.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 21 June 2005 and 12 April 2007 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Drawings

Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

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The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

The drawings submitted on 21 June 2005 are objected to because the requirements of 37 CFR 1.84(a)(2) have not been fulfilled. A petition has not been filed regarding the color drawings and referring to the amendment to the specification, filed 21 June 2005, indicating color drawings. .

Specification

The use of the trademark TET-ON (p. 12, line 20 and p.13, line 25) and has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claim 27 is objected to because of the following informalities: The term “respectively” is misplaced. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 is unclear with respect to the properties of the plurality of cells. The claim as recited indicates that a plurality of stably transfected cells inducibly expressing a plurality of catalytically active kinases from a single gene such that cells expressing a first kinase can be separated from a second kinase. It is unclear what property of the transfected gene encoding a plurality of kinases dictates the expression of a first kinase such that cells expressing the first kinase can be separated from cells expressing a second kinase if the plurality of kinases is encoded by a single gene. As suggested, but not explicitly, in line 6-7 of claim 27, an alternative interpretation is that each of the plurality of cells expresses a distinct kinase gene.

Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: A step of administering to the plurality of cells a plurality of compounds.

Claim 27 is further unclear because the claim does not indicate what result is considered false positive or false negative with respect to a plurality of compounds

Claim 27 is unclear with respect to the relationship between the frequency of false positives and false negatives against a plurality of compounds and the validity of a first data set or a second set of data.

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Claim 27 recites the limitation "inhibition data" in line 15. There is insufficient antecedent basis for this limitation in the claim.

Claims 28-30 also rejected because they depend from claim 27, and thus contain the above issues due to said dependence.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeung et al. (Molecular and Cellular Biology, Vol. 21, No. 21, p. 7207-7217, November 2001) in view of Welch et al. (JBC, Vol. 273, No. 18 p. 11248-11256, 1 May 1998) and in view of Technical bulletin No. 281 (Promega Corp., p. 1-13, 2002).

The claims are interpreted to be directed to a method of data processing comprising providing a first population of cells transfected with a reporter gene and a first inducible catalytically active kinase gene and a second population of cells transfected with a reporter gene and a second inducible, catalytically active kinase gene; acquiring a data set from cells expressing a first kinase and a data set from cells expressing a second kinase; calculating a frequency of false positives and false negatives against a plurality of compounds; and calculating inhibition data from the first and second data sets. In an embodiment, the data for the first kinase is analyzed or compared to the data for the second kinase that is in the same or different signaling pathway. In an embodiment the first and second kinases are in the same pathway selected from the group consisting of MEK-ERK pathway, IKK-NFkB pathway, p38 pathway, JNK-Jun pathway and JAK-STAT pathway.

Yeung et al. shows that the Raf kinase inhibitor can, in addition to inhibiting MEK-ERK pathway, inhibit the IKK-NFkB pathway. In figure 4, Yeung et al. shows that 293 cells are cotransfected with a reporter and with distinct kinases, NIK, NAK, TAK, MEKK, IKK, and p65. Yeung et al. shows the acquisition of data by measuring the level of

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reporter, luciferase (p. 7208, col. 2). As figure 4 shows luciferase activity was analyzed in cells expressing independently a first and second kinase. Yeung et al. shows the calculation of inhibition data from the first and second data elements by demonstrating an approximately five-fold inhibition of NIK and an approximately two-fold inhibition of TAK but no inhibition of NAK or MEKK (p. 7210, col. 2). In an embodiment, Yeung et al. shows the data for the first kinase is analyzed or compared to the data for the second kinase that is in the same or different signaling pathway. Yeung et al. shows that the kinases TAK, MEKK, and NIK are three kinases in the IKK-NFkB pathway (p. 7209, col. 2). In the experiments of figures 1 and 2, Yeung et al. is establishing, by refuting the null hypothesis that RKIP has no effect on NFkB signaling, conditions that would indicate false positive and false negative results and thereby validating the results of the subsequent data sets of figure 4. With respect to the null hypothesis that RKIP has no specific effect on NFkB signaling, a false positive result indicates that RKIP has an effect on NFkB signaling when it does not. Alternatively, the false negative result will indicate that RKIP has no effect on NFkB signaling when in reality it does. Yeung et al. address both possibilities in the series of experiments of figures 1 and 2 using a plurality of chemical compounds, Forskolin and U0126. Yeung et al. accomplishes this showing in figure 1a that sequestration of RKIP or overexpression the p65 subunit of NFkb induces expression of beta galactosidase from a NFkB dependent promoter. In figure 2, Yeung et al. shows that the MEK-ERK pathway inhibitor U0126 inhibits a reporter expressed from the control of a MEK-ERK specific promoter but does not inhibit the expression of the reporter under control of a non-MEK-ERK pathway promoter, SP1. In

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addition, Yeung et al. shows that while U0126 does decrease reporter expression under the control of NFkB by about 20%, RKIP in the presence or absence of U0126 inhibits expression of the NFkB driven reporter by about 90%. Together Yeung et al. uses the results of figures 1 and 2 to validate the experiment depicted in figure 4. Yeung et al. shows that the MEK-ERK pathway and the NFkB pathways are subject to crosstalk, suggesting that signaling of two kinases in different pathways could have an effect on reporter expression from each other.

Yeung et al. does not explicitly show than acquisition system inducible kinase expression.

Technical bulletin 281 regarding the Luciferase Assay System of Promega shows the detection of luciferase activity in cell lysates by an acquisition system. The bulletin shows that either a luminometer or scintillation counter can be used to measure luciferase activity in a sample (p. 7, section B). The bulletin shows the advantage of using a luminometer is that the as little as 10^{-20} moles of luciferase can be detected, which is equal to approximately 1 million molecules of luciferase. Thus the acquisition system provides sensitive detection of luciferase that would be insufficient for qualitative visual detection.

Welch et al. shows stable transfectants of gene constructs with inducible promoters. Welch et al. shows that the expression of gene constructs with inducible promoters can be controlled by the presences or absence of an inducer (fig 1).

It would have been obvious to one of ordinary skill in the art to modify the method of Yeung et al. with an acquisition system as in technical bulletin 281 because

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technical bulletin 281 shows the advantage of using a luminometer acquisition system is that the as little as 10^{-20} moles of luciferase can be detected. It would have been further obvious to modify the method of Yeung et al. to express kinases of interest from inducible constructs of Welch et al. because Welch et al. shows the advantage of the precise control of expression level.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571) 272-9047. The examiner can normally be reached on 8:00am-5:00pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/K. R. S./
Examiner, Art Unit 1631

18 August 2008
/John S. Brusca/
Primary Examiner, Art Unit 1631